

CLAIMS

1. A polynucleotide of any one of (a) to (d):

(a) a polynucleotide encoding a polypeptide comprising an amino acid sequence of any one of
5 SEQ ID NO: 2, 4, 6, or 8;

(b) a polynucleotide comprising the coding region of a nucleotide sequence of any one of SEQ
ID NO: 1, 3, 5, or 7;

(c) a polynucleotide encoding a polypeptide having an activity of causing a keratinocyte to
differentiate into a stratified epithelial cell when expressed in the keratinocyte, wherein the
10 polypeptide comprises an amino acid sequence with a substitution, deletion, insertion, and/or
addition of one or more amino acids in the amino acid sequence of any one of SEQ ID NO: 2, 4,
6, or 8; and

(d) a polynucleotide encoding a polypeptide having an activity of causing a keratinocyte to
differentiate into a stratified epithelial cell when expressed in the keratinocyte, wherein the
15 polynucleotide hybridizes under stringent conditions with a DNA comprising a nucleotide
sequence of any one of SEQ ID NO: 1, 3, 5, or 7.

2. The polynucleotide of claim 1 that is a gene involved in keratinocyte differentiation or
proliferation, wherein the polynucleotide encodes a secreted protein.

3. A polypeptide encoded by the polynucleotide of claim 1 or 2.

4. A vector into which the polynucleotide of claim 1 or 2 is inserted.

5. A host cell carrying the polynucleotide of claim 1 or 2 or the vector of claim 4.

6. A method for producing the polypeptide of claim 3, comprising the steps of culturing the host
cell of claim 5, and recovering a produced polypeptide from the host cell or its culture
supernatant.

7. A gene complex related to keratinocyte differentiation or proliferation, comprising each of (1)
a Kdap gene; (2) a dermokine- α gene; (3) a dermokine- β gene; and (4) a suprabasin gene,
wherein regulation of gene expression is commonly controlled.

8. A polynucleotide that hybridizes specifically with the polynucleotide of claim 1 or 2, wherein
the polynucleotide has a chain length of at least 15 nucleotides.

9. An antisense polynucleotide against the polynucleotide of claim 1 or 2, or a portion thereof.

10. An antibody that binds to the polypeptide of claim 3.

5 11. An agent for inducing keratinocyte differentiation, comprising a dermokine- α protein or a dermokine- β protein as an active ingredient.

12. An inhibitor of keratinocyte differentiation, comprising a compound selected from the group of (a) to (d):

- 10 (a) an antisense nucleic acid against a transcript of a dermokine- α gene or a dermokine- β gene;
(b) a nucleic acid having a ribozyme activity that specifically cleaves a transcript of a dermokine- α gene or a dermokine- β gene;
(c) a nucleic acid having an effect of inhibiting the expression of a dermokine- α gene or a dermokine- β gene through an RNAi effect; and
15 (d) an antibody that binds to a dermokine- α protein or a dermokine- β protein.

13. A method of screening for an inducer of keratinocyte differentiation, comprising steps (a) to (c):

- (a) contacting a cell that expresses a dermokine- α protein or a dermokine- β protein with a test
20 compound;
(b) measuring an expression level or an activity of a dermokine- α protein or a dermokine- β protein in the cell; and
(c) selecting a compound that increases the above expression level or activity, compared to in the absence of contact with the test compound.

25 14. A method of screening for an inhibitor of keratinocyte differentiation, comprising steps (a) to (c):

- (a) contacting a cell that expresses a dermokine- α protein or a dermokine- β protein with a test compound;
30 (b) measuring an expression level or an activity of a dermokine- α protein or a dermokine- β protein in the cell; and
(c) selecting a compound that decreases the above expression level or activity, compared to in the absence of contact with the test compound.

35 15. A method of screening for an inducer of keratinocyte differentiation, comprising steps (a) to (c):

(a) coexisting a test compound and a keratinocyte with a dermokine- α protein, a dermokine- β protein, or a cell expressing these proteins;

(b) measuring the differentiation of a keratinocyte into a stratified epithelial cell; and

(c) selecting a compound that increases differentiation into a stratified epithelial cell,
5 compared to in the absence of the test compound.

16. A method of screening for an inhibitor of keratinocyte differentiation, comprising steps (a) to (c):

(a) coexisting a test compound and a keratinocyte with a dermokine- α protein, a dermokine- β protein, or a cell expressing these proteins;
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(b) measuring the differentiation of a keratinocyte into a stratified epithelial cell; and

(c) selecting a compound that decreases differentiation into a stratified epithelial cell,
compared to in the absence of the test compound.

15 17. A method for examining whether or not a subject cell is a cancer cell derived from a stratified epithelium, comprising steps (a) and (b):

(a) measuring an expression level or an activity of a dermokine- α protein or a dermokine- β protein in a subject cell; and

(b) determining that the subject cell is a cancer cell derived from a stratified epithelium when
20 the above expression level or activity is different from a control.

18. A method for diagnosing a squamous epithelial cancer or a basal cell cancer in a subject, comprising steps (a) and (b):

(a) determining whether or not a cell sample prepared from a subject is a cancer cell derived
25 from a stratified epithelium, using the method of claim 17; and

(b) determining that the subject is affected with a squamous epithelial cancer or a basal cell cancer when the cell sample is determined to be a cancer cell derived from a stratified epithelium in the above step.

30 19. A method for diagnosing a skin disease in a subject, comprising steps (a) and (b):

(a) measuring an expression level or activity of a dermokine- α protein or a dermokine- β protein in a test sample prepared from a subject; and

(b) determining that the subject is affected with a skin disease when the above expression level or activity is different from a control.

35 20. The method for diagnosing of claim 19, wherein the skin disease is a xeroderma, psoriasis, or

ichthyosis.